

REMARKS

Applicants first note that the Examiner found Applicants' argument in the response filed on 12/17/04 persuasive, and that the restriction placed on former Groups III and IV has been withdrawn. The current Group IV encompasses all previous Group III and IV claims, except Claim 65, which now belongs to new Group V. Applicants also note that the Examiner has indicated that Claim 66 will be included in elected Group IV.

Applicants have amended Claim 48 to include the term "small molecule". Support for the term "small molecule" can be found, for example, in paragraphs [0091] and [0155] of the published US application US-20030165873-A1.

Applicants hereby elect Group IV, Claims 28-46, 48-55, 63, 64, and 66, *with traverse*. Applicants traverse this restriction requirement on the basis that the Groups are so closely related and they share common features that would facilitate searching all groups at once. For example, searching the subject matter of the polypeptides of Group I will necessarily entail the searching of subject matters claimed in Groups II – VI. Therefore, a search and examination of all pending claims can be made without imposing additional serious burden on the Examiner. Accordingly, reconsideration and withdrawal of the restriction requirement are respectfully requested.

Regarding the species election, Applicants hereby provisionally elect, *for search purposes only*, "methotrexate or a derivative thereof with minor structural modifications" for R1, "X represents O, and n = 5" for Y, and a small molecule "aromatic hydrocarbon" for R2, *with traverse*.

Applicants submit that species 1-3 subjected to election are encompassed by Markush groups. Applicants submit that all Markush group members can be examined simultaneously without significant additional burden on the Examiner. For example, the subject matter of the listed species (X represents O, S, SO, or SO₂) have closely related structures, and the total number of species (4) is sufficiently few that it would not constitute a significant additional burden to examine claims directed to all species simultaneously. In addition, Applicants respectfully point out that the search of the Markush-type claim will be extended to non-elected species should no prior art be found that anticipates or renders obvious the elected species (MPEP 803.02).

Applicants also note that all elected claims (Claims 28-46, 48-56, 63, 64 and 66) are generic claims encompassing all elected and non-elected species. Restrictions imposed on species encompassed by generic claims must be withdrawn upon indication of an allowable generic claim (MPEP 809). Presently, all elected claims (Claims 28-46, 48-56, 63, 64 and 66) read on the elected species 1-3.

In addition, regarding species election 3, Applicants first submit that the scope of R2 is not limited to “one of claim 1(i)(c) [sic] or one of claim 40,” as the Office Action suggests. In fact, Claim 28, for example, defines R2 as “a user-specified ligand.” To facilitate the *search*, however, Applicants elect a specifically recited small molecule, aromatic hydrocarbon, as a species of R2. Applicants submit that a species election for R2 is really unnecessary to search the claimed invention, particularly in view of the fact that this species election is on top of species elections regarding the other parts of the hybrid ligand R1-Y-R2. Applicants submit that a search using R1 as methotrexate or derivatives thereof already provides a sufficient focus for a clear search, and it does not seem to warrant further restriction for R2. There will be no additional search burden on the Examiner if this species election is withdrawn.

Regarding species election 4 (for “method steps”), Applicants hereby provisionally elect, *for search purposes only*, species “identifying a positive ligand binding cell in which an increase in the level of transcription of the reporter gene has occurred” (Claim 28 (iv)) of Group IV, *with traverse*. Applicants elect this species with traverse, because the basis for such a species election needs to be clarified. In particular, Applicants submit that steps (iii) and (iv) in Claim 28 are different steps of the *same* detection method. They are not meant to be performed as alternative means of detection, as the Office Action seems to suggest.

Even if the Office Action intends, for search purposes only, to restrict the various detection method steps, Applicants submit that the different detection method steps are sufficiently few (the Examiner requests an election between only two alleged species) that no undue search burden would be imposed on the Examiner to search all species simultaneously.

Applicants note that at least Claims 46 and 48-55 are generic claims encompassing all elected and non-elected species. Restrictions imposed on species encompassed by generic claims

must be withdrawn upon indication of an allowable generic claim (MPEP 809). Presently, Claims 28-42, 46, 48-56, and 66 read on the elected species.

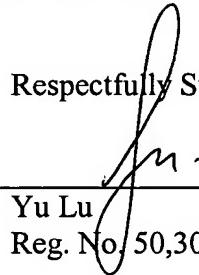
Applicants further traverse the species election requirements because it is plain that no significant search burden would be placed on the Examiner by examining the entirety of the elected claims as written. In fact, the related continuation-in-part application USSN 10/234985, filed on September 3, 2002, in which an Office Action has issued, includes claims that recite similar variables with similar options, yet were not subjected to any such species election. The Office Action in that case was prepared by the examiner with no apparent difficulty and with no narrowing of focus to one or more particular species within the claim scope as is being required of Applicants in the present case. Accordingly, it is apparent that it must not be an undue burden to search more broadly than the requirement of election of species suggests.

In summary, although Applicants have made the required group and species elections, Applicants submit that no additional search burden would be imposed on the Examiner if one or more of these group or species elections were withdrawn. This is particularly true for the species election. Reconsideration and withdrawal of the group and species elections are thus respectfully requested.

CONCLUSION

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,


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